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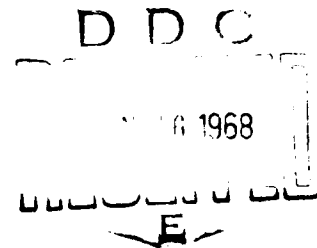
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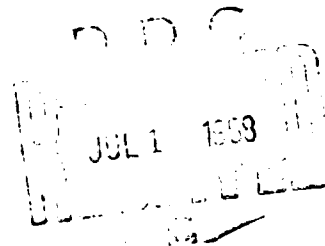
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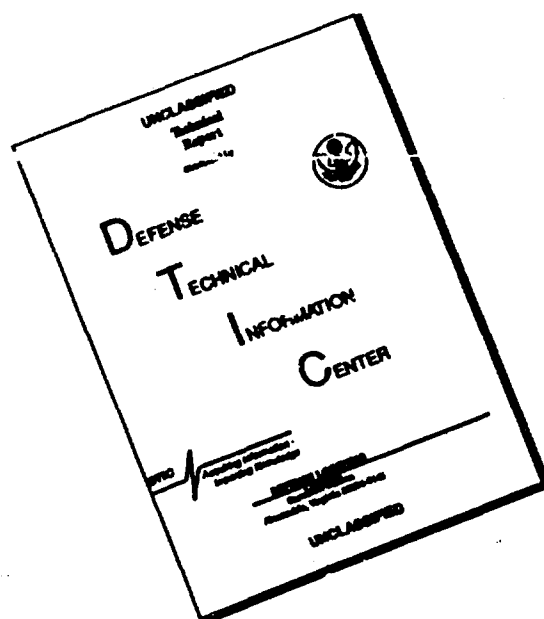
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THE CLINICAL SIGNIFICANCE OF AUTOIMMUNE
REACTIONS IN THYROPATHIES

Minerva Med.
(Medical Minerva)
Vol 56, 1965, pp 1821,1827-29

Mario Austoni
Donato Ziliotto

(The immunological research which is the basis of this report was accomplished with the help of the funds made available by the National Research Council (Endocrinology Division, Thyroid Group) to the Institute of Semiotic Medicine of the University of Padua in 1959-1965.)

The discovery of the autoimmune phenomenon, although rather recent, immediately turned out to be so important as to revolutionize entire sectors of human pathology; Dameshek (1961) shows that autoimmune diseases are destined to constitute a new group of diseases of importance comparable to that of the infectious diseases, the hereditary diseases, and the neoplastic diseases.

This concept, which asserted itself first of all primarily because of the achievements in immunohematology, is immediately picked up in the field of thyropathies with the pathogenetic interpretation of lymphomatous thyroiditis of Hashimoto, which from then on was considered as a model of autoimmunopathy.

Here the principal antigen is made up of thyroglobulin, a substance usually "secreted" by the organism but capable of sensitizing it if, issuing from the follicle, it comes into contact with immunologically competent cells.

Nowadays, the doctrinal, experimental, and clinical developments and discoveries are so irrelevant as not only to make a revision of the entire thyroid nosography necessary, but also to propose diagnostic and therapeutic applications of great interest. In spite of this, the clinical-diagnostic significance of the autoimmune reactions is not entirely secure in this case; the demonstration of circulating antibodies so far is the

only method of proving the existence of an autoimmune state; but this method cannot yet be considered as the decisive method although it is true that considerable auto-antibody rates are found in almost all of the thyropathies and even in normal persons or in diseases of an entirely different nature. This has generated the doubt, that in contrast to what was thought to be the case initially, the circulating antibodies do not express the existence of an autoaggressive process in all cases. However it seemed to us to be a good idea to re-examine this issue on the basis of numerous data in the literature and a vast personal case history background; we were able to do this with the help of the foresighted initiative of the National Research Council; this enabled us to study the clinical significance of autoimmune reactions in a broad range of thyropathies, with particular emphasis on those postulated by autoaggressive genesis as presumed to be such.

This fits quite nicely into the treatment of thyroid tumors for at least four reasons:

- (1) we often find auto-antibodies even in the thyroid tumors;
- (2) according to Roitt and Doniach (1960), the different level of antibodies in cancer and in Hashimoto disease has a differing diagnostic value in these two diseases;
- (3) according to Lindsay (1960), Hashimoto disease often coexists with tumors or evolves in this sense;
- (4) according to Witebsky and associates (1956), thyroid cancer is perhaps the only tumor which "keeps an antigenic structure strictly correlated with that of the normal thyroid."

(d) Method of Fluorescent Antibodies (Coons and Kaplan). This method makes use of the principle of marking the antibodies with a fluorescent substance (isothiocyanate fluoresceine) and of using the serum thus treated as a histological coloring agent on frozen sections of thyroid. In the place where the reaction occurs, we can observe a bright yellow-green coloration under the fluorescence microscope.

We mostly use the "indirect" technique which consists in making the nonconjugated sera being examined react with the thin slice; the latter is then treated with a conjugate of fluoresceine and of human anti-gamma-globulin serum which is fixed on the antibodies in the place where they reacted with the corresponding thyroid antigen. This technique enables us to examine in a short time a large number of sera, such as Doniach and Roitt used it as a preliminary examination for all of the sera, both for the thyroid and for the other tissues (stomach). Others (Potter and Fennell, 1961) however observed that the indirect technique reveals "so much aspecific [nonspecific] fluorescence as to turn out to be unsatisfactory." With this technique we can then demonstrate both the antibodies located in the colloid (thyroglobulin and CA2) and those in the cells. In the first case the sections must be fixed with formalin or methanol because

the colloid is removed by the water. If, instead, we want to demonstrate the cellular antigens, the thin slices must not be fixed because the fixing agents alter the antigens.

Looking for Gastric Anti-Mucosa Antibodies. These are directed against antigens contained in the microsomic fraction of the parietal cells of the gastric mucosa. They are established with the help of the technique of the complement fixation reaction, involving a procedure similar to that used for the thyroid antibodies, employing as antigen, in this case, a whole saline extract of mucosa of the bottom of the stomach. We also can use the technique of fluorescent antibodies on nonfixed sections of the stomach.

Looking for Nonorgano-Specific Antibodies. Anti-nuclear antibodies. We look for these using the technique of immunofluorescence; we employ sections of human thyroid or of rat liver, not fixed. In our laboratory we also use the technique of the complement fixation [reaction], employing as antigen DNA, diluted 1:100 in a buffer [solution] of phosphates with a pH of 7.2.